

Amendments To The Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

1. (Original) A method of forming a compound of the general formula, Ar-R, the method comprising:
contacting a mixture of an aryl substrate with a nucleophilic leaving group, an organozinc species capable of transmetalation and a metal complex capable of effecting the coupling of an aryl substrate and an organozinc species to synthesize a compound of the formula Ar-R where Ar is an aryl or heteroaryl group and R is an aralkyl, arylmethyl or a (heteroaryl)methyl group.
2. (Currently Amended) A method of claim 31, wherein the metal complex is a nickel, palladium or platinum complex.
3. (Original) A method of forming a compound of the general formula, Ar-R, the method comprising the step of
contacting a mixture of aryl halide, ArX, and an organozinc species, RZnY, in the presence of at least a catalytic amount of a palladium complex under conditions conducive to the formation of an Ar-R bond, wherein:
Ar is optionally substituted phenyl, optionally substituted 1-naphthyl, optionally substituted 2-naphthyl, or optionally substituted heteroaryl having from 5 to about 18 ring atoms, 1 to about 3 rings and 1 to about 4 ring heteroatoms selected from N, O or S;
R is optionally substituted aralkyl;
X is Cl, Br, I, arylsulfonate, alkylsulfonate or triflate; and
Y is F, Cl, Br, I, arylsulfonate, alkylsulfonate or triflate.

4. (Original) A method of claim 3, wherein Ar-R bond formation is effected by a palladium mediated cross-coupling reaction.
5. (Original) A method of claim 3, wherein the mixture is dissolved in an inert solvent selected from hydrocarbons, aromatic hydrocarbons, chlorinated hydrocarbons, or oxygenated hydrocarbons.
6. (Original) A method of claim 3, wherein the mixture is dissolved in an inert solvent selected from diethyl ether, *tert*-butylmethylether, tetrahydrofuran, dioxane, dioxolane, benzene, toluene, ethylbenzene or xylenes;
7. (Original) A method of claim 3, wherein the mixture is dissolved in an inert solvent so the aryl halide, ArX, is present in about 0.01 M to about 2 M.
8. (Original) A method of claim 3, wherein the mixture is dissolved in an inert solvent so the aryl halide, ArX, is present in about 0.1M to about 1 M.
9. (Currently Amended) A method of ~~any one of claims 3 to 8~~claim 3, wherein the mixture is heated to a temperature between about 25°C and about 150°C.
10. (Currently Amended) A method according to ~~any one of claims 3 to 8~~claim 3, wherein the mixture is heated to a temperature between about 30°C and about 110 °C.
11. (Currently Amended) A method of ~~any one of claims 3 to 8~~claim 3, wherein the mixture is heated to a temperature where the inert solvent refluxes.
12. (Currently Amended) A method of ~~any one of claims 3 to 11~~claim 3, wherein formation of a cross-coupled product, Ar-R, occurs between about 1 minute and about 48 hours.

13. (Currently Amended) A method of ~~any one of claims 3 to 11~~claim 3, wherein formation of a cross-coupled product, Ar-R, occurs between about 5 minutes and about 16 hours.

14. (Currently Amended) A method of ~~any one of claims 3 to 11~~claim 3, wherein formation of a cross-coupled product, Ar-R, occurs between about 10 minutes and about 4 hours.

15. (Currently Amended) A method of ~~any one of claims 3 to 14~~claim 3, wherein at least 50 mole % of Ar-X is converted into a cross-coupled product.

16. (Currently Amended) A method of ~~any one of claims 3 to 14~~claim 3, wherein at least 75 mole % of Ar-X is converted into a cross-coupled product.

17. (Currently Amended) A method of ~~any one of claims 3 to 14~~claim 3, wherein at least 90 mole % of Ar-X is converted into a cross-coupled product.

18. (Currently Amended) A method of ~~any one of claims 3 to 14~~claim 3, wherein at least 95 mole % of Ar-X is converted into a cross-coupled product.

19. (Original) A method of claim 3, wherein the palladium catalyst is a L_2Pd complex which may comprise additional ligands bound to palladium, and L is phosphite or phosphite or L_2 taken in combination is chelating ligand selected from bis(phosphine), bis(phosphite), phosphine-phosphite or 2,2'-bipyridine derivative.

20. (Original) A method of claim 19, wherein L_2 is optionally substituted 1,1'-bis(diarylphosphino)-ferrocene, optionally substituted 2,2'-bis(diarylphosphino)-binaphthyl, optionally substituted 2,2'-bis(diarylphosphino)-biphenyl, optionally substituted α,ω -bis(diarylphosphino)- C_{1-6} alkylene, optionally substituted 1,2-bis(di- C_{1-6} alkylphosphino)benzene, or 2,2'-bis(diarylphosphino)-diarylether.

21. (Original) A method of claim 19, wherein
L₂ is 1,1'-bis(diarylphosphino)-ferrocene, 2,2'-bis(diarylphosphino)-binaphthyl, or
2,2'-bis(diarylphosphino)-diphenylether; and
aryl is phenyl, 2-tolyl, 3-tolyl, or 4-tolyl.

22. (Original) A method of claim 19 wherein the palladium catalyst is
selected from
L₂PdZ₂ precursor complexes where L is defined in claim 16 and Z is Cl, Br, or I;
or the palladium catalyst is generated *in situ* from a mixture of a palladium source
selected from palladium chloride, palladium bromide, palladium acetate, L^{*}_nPd wherein
L^{*} is phosphine, amine, ether, thiophene, alkene, alkyne or a mixture thereof; and
and n is between about 2-4.

23. (Original) A method of claim 22, wherein the palladium catalyst is
selected from L₂PdCl₂, L₂PdBr₂, and mixtures of Pd(alkene)_n and L₂, a chelating
bis(phosphine), wherein
alkene is selected from dibenzylidene acetone, norbornadiene, 1,5-cyclooctadiene,
and ethylene such that 3 or 4 C=C bonds are coordinated to Pd; and
L₂ is selected from 1,1'-bis(diarylphosphino)-ferrocene, 2,2'-bis(diarylphosphino)-
binaphthyl, or 2,2'-bis(diarylphosphino)-diphenylether.

24. (Original) A method of claim 23, wherein the mixture of Pd(alkene)_n
and L₂, a chelating bis(phosphine) has a molar ratio of Pd to L₂ between about 1:1 and
about 1:3.

25. (Original) A method of claim 23, wherein the mixture of Pd(alkene)_n
and L₂, a chelating bis(phosphine) has a molar ratio of Pd to L₂ between about 1:1 and
about 1:1.5.

26. (Currently Amended) A method of ~~any one of claims 19 through 25~~claim 19, wherein the palladium catalyst loading is less than about 25 mole % relative to the Ar-X component.

27. (Currently Amended) A method of ~~any one of claims 19 through 25~~claim 19, wherein the palladium catalyst loading is less than about 10 mole % relative to the Ar-X component.

28. (Currently Amended) A method of ~~any one of claims 19 through 25~~claim 19, wherein the palladium catalyst loading is less than about 5 mole % relative to the Ar-X component.

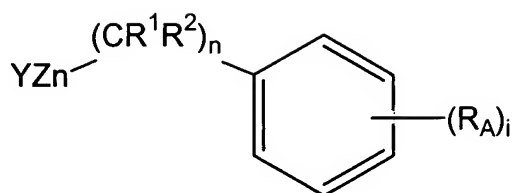
29. (Currently Amended) A method of ~~any one of claims 19 through 25~~claim 19, wherein the palladium catalyst loading is less than about 2 mole % relative to the Ar-X component.

30. (Original) A method of claim 3, wherein the molar ratio of the Ar-X component to the RZnY component is between about 1:1 and about 1:10.

31. (Original) A method of claim 3, wherein the molar ratio of the Ar-X component to the RZnY component is between about 1:1.5 and about 1:5.

32. (Original) A method of claim 3, wherein the molar ratio of the Ar-X component to the RZnY component is between about 1:1.5 and about 1:3.

33. (Original) A method of claim 3, wherein RZnY is an organozinc compound of formula II:



II

wherein

Y is as defined in claim 3;

R^1 and R^2 are independently selected at each occurrence of R^1 and R^2 from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, or C_{3-8} cycloalkyl;

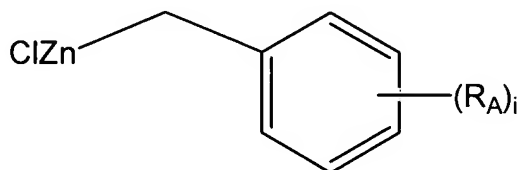
R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, chloro, fluoro, C_{1-4} fluoroalkyl, amino, mono and di(C_{1-6} alkyl)amino, nitrile, optionally substituted aryloxy, optionally substituted heteroaryloxy, C_{1-6} alkylthio, optionally substituted arylthio, optionally substituted heteroarylthio, optionally substituted aryl acetoxy or optionally substituted heteroaryl acetoxy; or

two R_A groups on adjacent ring atoms taken in combination form a second ring optionally comprising zero, one or two hetero ring atoms;

n is an integer from 1 to about 4; and

i is an integer from 0 to 5.

34. (Original) A method of claim 33, wherein $RZnY$ is an organozinc compound of formula III:



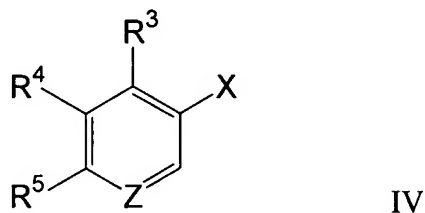
III

wherein:

R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, chloro, fluoro, C_{1-4} alkyl, C_{1-4} alkoxy, and C_{1-2} fluoroalkyl;

i is an integer from 0 to about 3.

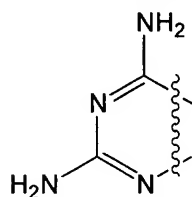
35. (Original) A method of claim 3, wherein the aryl halide, ArX, is a compound of Formula IV:



wherein:

R⁴ and R⁵ are independently selected from the group consisting of hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, chloro, fluoro, C₁₋₆fluoroalkyl, C₁₋₆alkoxy, amino, mono and di(C₁₋₆alkyl)amino, and nitrile; or

R⁴ and R⁵ taken in combination form a group of the formula:



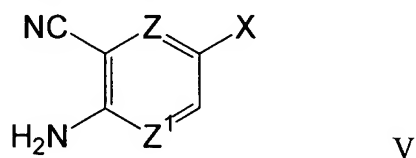
X is I or Br; and

Z is N or CR³;

Z¹ is N or CH; and

R³ is hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, chloro, fluoro, C₁₋₆fluoroalkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, optionally substituted arylthio, or optionally substituted arylalkylthio.

36. (Original) A method of claim 35, wherein the aryl halide, ArX, is a compound of Formula V:



wherein:

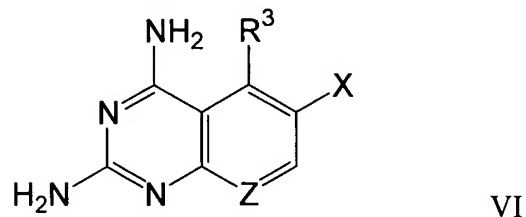
X is Br or I;

Z is N or CR³;

Z^1 is N or CH; and

R^3 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, chloro, fluoro, C_{1-6} fluoroalkyl, or C_{1-6} alkoxy.

37. (Original) A method of claim 35, wherein the aryl halide, ArX , is a compound of Formula VI:



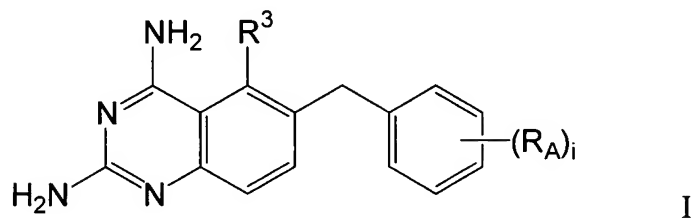
wherein:

X is Br or I;

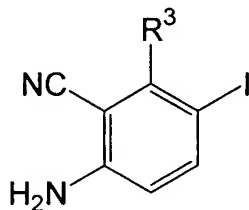
Z is N or CH; and

R^3 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, chloro, fluoro, C_{1-6} fluoroalkyl, or C_{1-6} alkoxy.

38. (Original) A method of forming a compound according to Formula I:



the method comprising the steps of
contacting an aryl halide of the formula:



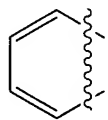
with at least one molar equivalent of an organozinc reagent, $RZnY$, and at least a catalytic amount of a palladium catalyst under conditions conducive to the formation of an C-C bond by a palladium mediated cross-coupling reaction;

contacting the product of the cross-coupling reaction with chloroformamidine under dry-fusion conditions conducive to formation of a compound according to Formula I, wherein

R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, chloro, fluoro, C_{1-4} fluoroalkyl, amino, mono and di(C_{1-6} alkyl)amino, nitrile, optionally substituted aryloxy, optionally substituted heteroaryloxy, C_{1-6} alkylthio, optionally substituted arylthio, optionally substituted heteroarylthio, optionally substituted aryl acetoxy or optionally substituted heteroaryl acetoxy; or

or

two adjacent R_A groups taken in combination form a group of the formula:

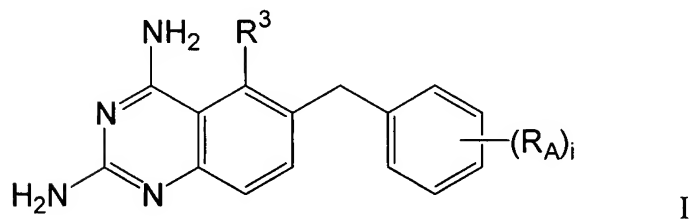


which may be optionally substituted;

R^3 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, chloro, fluoro, C_{1-6} fluoroalkyl, or C_{1-6} alkoxy; and

Y is Cl, Br, I, or triflate.

39. (Original) A compound according to Formula I:

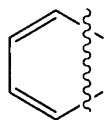


wherein:

R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, chloro, fluoro, C_{1-4} fluoroalkyl, amino, mono and di(C_{1-6} alkyl)amino, nitrile, optionally substituted

aryloxy, optionally substituted heteroaryloxy, C₁₋₆alkylthio, optionally substituted arylthio, optionally substituted heteroarylthio, optionally substituted aryl acetoxy or optionally substituted heteroaryl acetoxy; or

two adjacent R_A groups taken in combination form a group of the formula:



which may be optionally substituted;

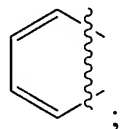
R³ is hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, chloro, fluoro, C₁₋₆fluoroalkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, optionally substituted arylthio, or optionally substituted arylalkylthio; and

i is an integer from 0 to about 5.

40. (Original) A compound according to claim 39, wherein the compound is a lipophilic inhibitor of dihydrofolate reductase.

41. (Original) A compound of claim 39 wherein R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, chloro, fluoro, C₁₋₄alkyl, C₁₋₄alkoxy, and C₁₋₂fluoroalkyl; or

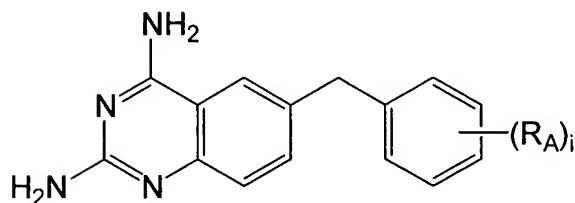
two adjacent R_A groups taken in combination form a group of the formula:



R³ is hydrogen, methyl, chloro or fluoro; and

i is an integer from 0 to about 3.

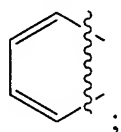
42. (Original) A compound of claim 39 according to Formula I-A:



I-A

wherein

R_A is independently selected at each occurrence from the group consisting of hydrogen, fluoro, chloro, methoxy, methyl, and trifluoromethyl; or two adjacent R_A groups taken in combination form a group of the formula:



i is an integer from 0 to about 3.

43. (Currently Amended) A pharmaceutical composition comprising a compound of ~~any one of claims 39 through 42~~ claim 39 and a pharmaceutically acceptable carrier.

44. (Currently Amended) A method for treating a mammal suffering or susceptible to a parasitic infection or disorder, comprising administering to the mammal an effective amount of a compound or composition of ~~any one of claims 39 through 43~~ claim 39.

45. (Original) A method of claim 44 wherein the mammal is immuno-compromised.

46. (Currently Amended) The method of claim ~~44 or claim 45~~, wherein the mammal is HIV-positive.

47. (Currently Amended) The method of ~~any one of claims 44 through 46~~ claim 44, wherein the mammal is suffering from an acquired immune deficiency disorder.

48. (Original) The method of claim 44, wherein the mammal is suffering from an autoimmune disorder or disease.

49. (Currently Amended) The method of ~~any one of claims 44 through 48~~claim 44, wherein the mammal has a parasitic infection.

50. (Original) The method of claim 49, wherein the parasitic infection is a *Pneumocystis carinii* (Pc) and *Toxoplasma gondii* infection.

51. (Currently Amended) A method for treating an immuno-comprised mammal comprising administering to the mammal an effective amount of a compound or composition of ~~any one of claims 39 through 43~~claim 39.

52. (Original) The method of claim 51, wherein the mammal is HIV-positive.

53. (Original) The method of claim 51, wherein the mammal has AIDS.

54. (Original) The method of claim 51, wherein the mammal has an autoimmune disorder.

55. (Currently Amended) The method of claim ~~44 through 54~~ wherein the mammal is a human.